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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/725,906 | 11/30/2000 | Lisa McKerracher | 06447-003-US-02 | 9776 |

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| EXAMINER | |
|---|---|
| WEGERT, SANDRA L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | |

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/725,906 | MCKERRACHER, LISA | |
| | Examiner | Art Unit | |
| | Sandra Wegert | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *3,6 and 8-18* is/are pending in the application.

4a) Of the above claim(s) *3,6 and 8-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Application, Amendments, and/or Claims*

The Supplemental Information Disclosure Statement, sent 7 April 2004, has been entered into the record. The amendment filed 7 April 2004 has been entered. Claims 3, 6 and 8-10 are withdrawn. Claims 1, 2, 4, 5 and 7 are canceled. Claims 11-18 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office action.

### *Withdrawn Objections and/or Rejections*

### Informalities

#### *Figures*

The objection to Figure 9 for missing text, as set forth in the previous Office Action (21 January 2004), is *withdrawn* in view of the amendment which added explanatory text to the figure (7 April 2004).

#### *Sequence Rules*

The objection to the instant Specification for lacking sequence identifiers, as set forth in the previous Office Action (21 January 2004), is *withdrawn* in view of the amendment which added SEQ ID NO's to sequences listed on pages 41-43 of the Specification (7 April 2004).

**35 *USC § 112, second paragraph, indefiniteness***

The rejection of Claims 1, 2, 3, 5 and 6 under 35 U.S.C. 112, second paragraph, for reciting indefinite claim language, is *withdrawn*. Applicants have added the phrase "axonal sprouting" to new Claims 11-18, as is commonly recited in the literature (see for example: Masuda-Nakagawa, L., et al, 1993, PNAS, 90: 4966-4970).

***35 USC § 102- Prior Art***

The rejection of Claims 1, 2 and 4 under 35 USC 102(b) is withdrawn. Applicants have introduced new claims 11-18 which enumerate the components of the instant invention, thereby distinguishing it from that described by Redl, et al (US Patent 4,631,055 23 December 1986). The added claims list the compositions of injected proteins, as well as better describes the matrix (7 April 2004).

***Maintained Objections and/or Rejections***

***Claim Rejections - 35 USC § 112, first paragraph, scope of enablement***

Claims 11-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an axon-elongation stimulation kit comprising *C3 exoenzyme* at tested concentrations (e.g., corresponding to a final *in situ* concentration of 25-50μg/ml), combined in a gel matrix with "fibrin sealant" (comprising fibrinogen concentrate, calcium chloride, thrombin and protease inhibitors) and with a matrix formed from well-defined components, is not enabled

for an axon-growth stimulation kit comprising two or more containers containing components *being capable once intermingled of forming a flowable carrier component.* This rejection was made previously for Claims 1, 2, 3, 4, 5 and 7 (Claim 7 was incorrectly listed instead of Claim 6) as directed to components "capable of forming a therapeutically acceptable matrix."

Claims 11-18 recite or encompass a *property* of the matrix-forming apparatus ("being capable once intermingled of forming a flowable carrier component") without reciting the elements that would impart that property to the apparatus or chemical solution. The fact that the claims recite a property without reciting the specific means of achieving that property, results in claims that encompass every conceivable apparatus and chemical formula that would produce a matrix with that property (see MPEP § 2164.08(a), based on Hyatt, 708 F.2d 712, 714-715, 218 USPQ 195, 197 (Fed. Cir. 1983)). This means necessarily that the scope of protection encompassed by the claims is not commensurate with the scope of enablement provided by the Specification.

The specification is not enabled for the full scope of the claimed apparatus or chemical solution with the assurance that the apparatus/chemical components claimed can be made and used without undue experimentation and with the assurance that it would have the desired properties. There are no examples of what specific compounds would be used in the invention or fall within the range of those that would be included and still be useful for facilitating axon growth. Furthermore, the field of neural development is not well-established in terms of clearly defining the specific series of compounds and steps involved in causing axon elongation in vivo. For example, many classes of compounds, including cytoskeletal proteins, growth factors and growth-inhibiting factors are involved in *in vivo* guidance of each axon, at least during

development (Zigmond, M.J., editor, 1999, Fundamental Neuroscience, Academic Press, pages 526-543). Still less is known about axon elongation after injury in adult animals, but since central nervous system axon growth is rarely seen after injury in adults, it can be assumed that there exist barriers to such growth and that such means of facilitating axon elongation after injury are not well-known to researchers. Since Claims 11-18 read on any apparatus or chemical solution that is "capable once intermingled of forming a flowable carrier componenet," they read on all developments in the axon-sprouting field that have the cited properties, including those that have not been invented yet. The claims also read on any combination of apparatus and chemical componenets that are mixed with any thixotrope to form a matrix for in vivo application.

Proper analysis of the Wand's factors were provided in the previous Office Action. Due to the large quantity of experimentation required to determine how to use the apparatus described to stimulate axon growth, the lack of direction or guidance in the specification regarding same - e.g., the lack of guidance regarding use of components other than *C3* exoenzyme or Y-27632, combined with the "fibrin sealant" matrix, the lack of working examples to all variants of the claimed components, the state of the art showing the many types of compounds that can cause axon elongation, the unpredictability of function of most injected compounds in terms of causing axon elongation, and the breadth of the claims which embrace innumerable compounds defined only vaguely and only in terms of function- undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

***35 USC § 112, first paragraph – Written Description.***

Claims 13, 15 and 18 are rejected under 35 USC § 112, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This rejected was previously made over Claims 1, 2, 3, 5 and 6 (18 October 2003).

Claims 13, 15 and 18 are directed to an axon growth stimulation kit comprising a compartment or compartments and proteins or chemicals capable of forming a flowable carrier component for facilitating axon growth at a site of injury in vivo. The specification teaches use of matrix forming components and *C3* exoenzyme to form a biocompatible axon-elongation gel that adheres well to the growing nerve and stimulates and guides axonal lengthening. There are a limited number of closely related C3 exoenzymes known in the art (Hauser, et al, 1993, J. Bacteriol., 175(22): 7260-7268; Moriishi, et al, 1993, Infection and Immunity, 61(12): 5309-5314). In addition, Y-27632, a rho-kinase inhibitor functionally-similar to C3 exoenzyme has been discussed in the literature in terms of regulating the growth of epithelial cells (Omelchenko, et al, 2003, PNAS, 100(19): 10788-1079). However, the specification does not teach functional or structural characteristics of all compounds used in the kit. Use of a "C3 analogue," for example other than those enumerated above -for example, C3-C, C3-D and Y-27632, described only as capable of inactivating Rho GTPase, is not adequate written description of an entire genus of functionally equivalent compounds that stimulate axon growth or form a flowable matrix.

With the exception of C3-C, C3-D and Y-27632, the skilled artisan cannot envision the

detailed chemical structure of the encompassed compounds, and therefore, would not know how to make or use them. The description of one Rho-kinase inhibitor polypeptide species is not adequate written description of an entire genus of functionally equivalent compounds that may include a variety of chemical genera. Applicants have not made and tested all possible encompassed Rho kinase inhibitors, nor even tested a representative subset of possible encompassed ligands, and shown they function identically in the claimed methods.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a recitation of the name of the Rho kinase ligand used for the claimed methods. In the absence of a sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Making and using a representative number of Rho kinase ligands are likewise not adequately described.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion: Claims 11-18 are rejected for the reasons listed above.

**Advisory information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW

15 July 2004

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER